

IV

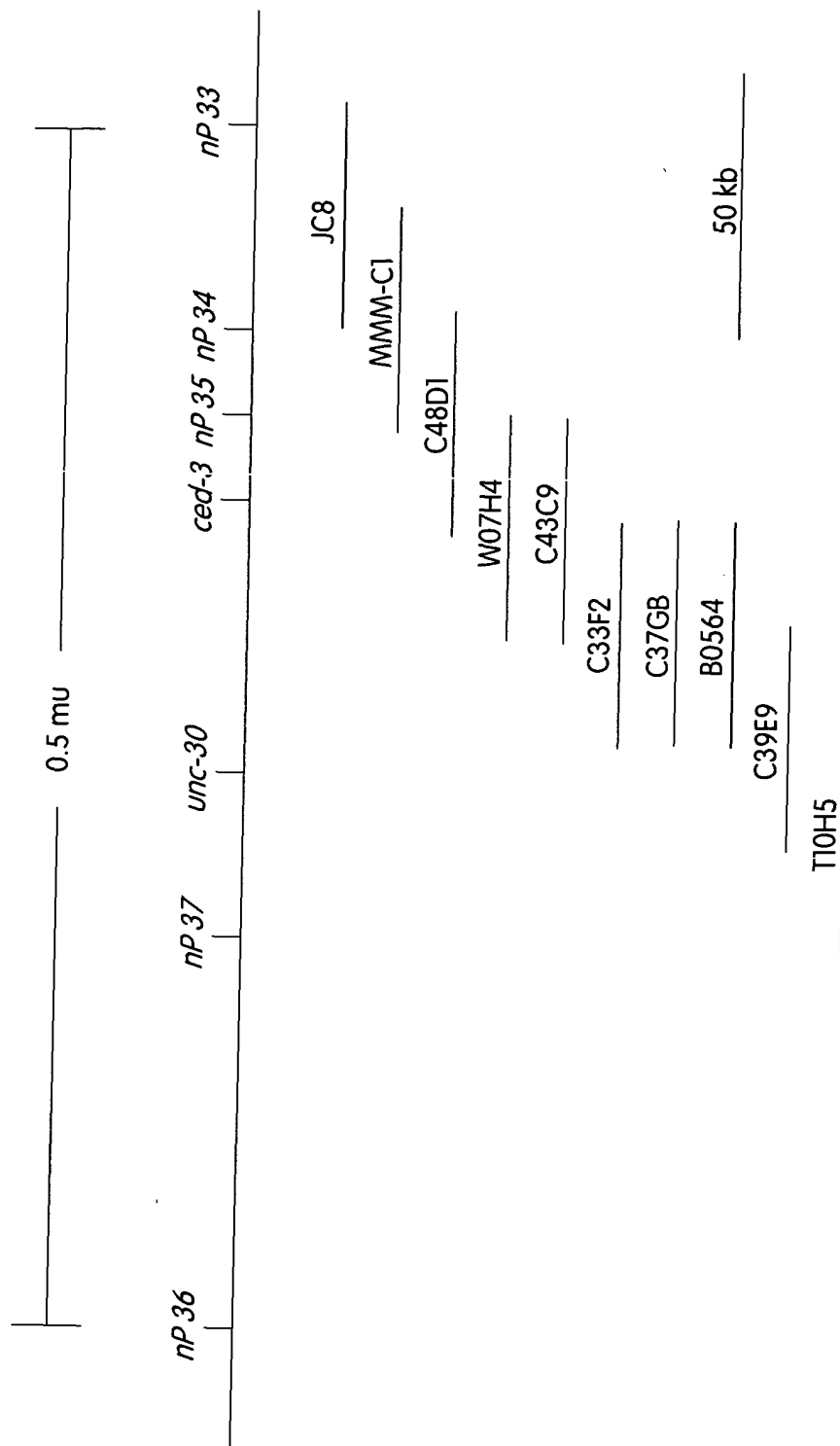


Fig. 1

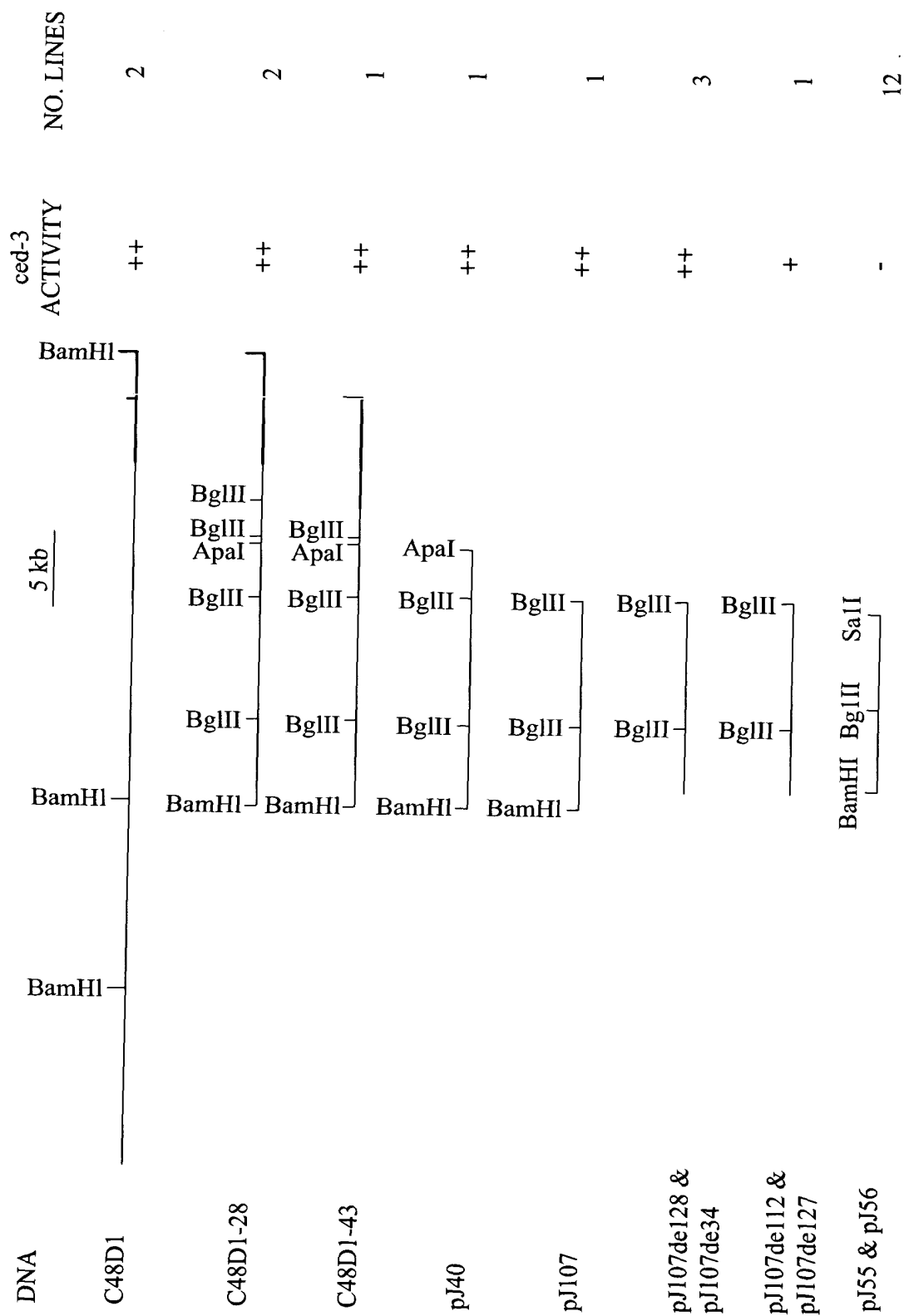


Fig. 2

*ced-3* Genomic Sequence

AGATCTGAAATAAGGTGATAAATTAATAAATTAAGTGTATTTCTGAGGAAATTTGACTGT  
 1 -----+-----+-----+-----+-----+-----+ 60  
 TTTAGCACAAATTAATCTTGTTCAGAAAAAAGTCCAGTTTCTAGATTTTCCGTCTTA  
 61 -----+-----+-----+-----+-----+-----+ 120  
 TTGTCGAATTAATATCCCTATTATCACTTTTTCATGCTCATCCTCGAGCGGCACGTCCTC  
 121 -----+-----+-----+-----+-----+-----+ 180  
 AAAGAATTGTGAGAGCAAACGCGCTCCCATTGACCTCCACACTCAGCCGCCAAAACAAAC  
 181 -----+-----+-----+-----+-----+-----+ 240  
 GTTCGAACATTTCGTGTGTTGTGCTCCTTTTCCGTTATCTTGCAGTCATCTTTTGTCTGTT  
 241 -----+-----+-----+-----+-----+-----+ 300  
 TTTTCTTTGTTCTTTTGTGAACGTGTTGCTAAGCAATTATTACATCAATTGAAGAAAA  
 301 -----+-----+-----+-----+-----+-----+ 360  
 GGCTCGCCGATTTATTGTTGCCAGAAAGATTCTGAGATTCTCGAAGTCGATTTTATAATA  
 361 -----+-----+-----+-----+-----+-----+ 420  
 TTTAACCTTGGTTTTTGCATTGTTTCGTTTAAAAAAACCACTGTTTATGTGAAAAACGA  
 421 -----+-----+-----+-----+-----+-----+ 480  
 TAGTTTACTAATAAACTACTTTTAAACCTTTACCTTTACCTCACCGCTCCGTGTTTCATG  
 481 -----+-----+-----+-----+-----+-----+ 540  
 GCTCATAGATTTTCGATACTCAAATCCAAAAATAAATTTACGAGGGCAATTAATGTGAAA  
 541 -----+-----+-----+-----+-----+-----+ 600  
 CAAAAACAATCCTAAGATTCCACATGTTTGACCTCTCCGGCACCTTCTTCTTAGCCCC  
 601 -----+-----+-----+-----+-----+-----+ 660  
 ACCACTCCATCACCTCTTTGGCGGTGTTCTTCGAAACCCACTTAGGAAAGCAGTGTGTAT  
 661 -----+-----+-----+-----+-----+-----+ 720  
 CTCATTTGGTATGCTCTTTTCGATTTTATAGCTCTTTGTGCGCAATTTCAATGCTTTAAAC  
 721 -----+-----+-----+-----+-----+-----+ 760  
 AATCCAAATCGCATTATATTTGTGCATGGAGGCAAATGACGGGGTTGGAATCTTAGATGA  
 781 -----+-----+-----+-----+-----+-----+ 840  
 GATCAGGAGCTTTTCAGGGTAAACGCCCGGTTTCATTTTGTACCACATTTTCATCATTTTCT  
 841 -----+-----+-----+-----+-----+-----+ 900  
 GTCGTCCTTGGTATCCTCAACTTGTCCCGGTTTTGTTTTTCGGTACACTCTTCCGTGATGC  
 901 -----+-----+-----+-----+-----+-----+ 960  
 CACCTGTCTCCGTCTCAATTATCGTTTAGAAATGTGAACTGTCCAGATGGGTGACTCATA  
 961 -----+-----+-----+-----+-----+-----+ 1020  
 TTGCTGCTGCTACAATCCACTTTCTTTTCTCATCGGCAGTCTTACGAGCCCATCATAAAC  
 1021 -----+-----+-----+-----+-----+-----+ 1080  
 TTTTTTTTCCGCGAAATTTGCAATAAACCGGCCAAAACTTTCTCCAAATTGTTACGCAA  
 1081 -----+-----+-----+-----+-----+-----+ 1140  
 TATATACAATCCATAAGAATATCTTCTCAATGTTTATGATTCTTCGCAGCACTTTCTCT  
 1141 -----+-----+-----+-----+-----+-----+ 1200  
 TCGTGTGCTAACATCTTATTTTATAATATTTCCGCTAAAAATCCGATTTTGTAGTATTA  
 1201 -----+-----+-----+-----+-----+-----+ 1260  
 ATTTATCGTAAAATTATCATAATAGCACCGAAAACTACTAAAAATGGTAAAAGCTCCTTT  
 1261 -----+-----+-----+-----+-----+-----+ 1320

Repeat 1

TAAATCGGCTCGACATTATCGTATTAAGGAATCACAAAATCTGAGAATGCGTACTGCGC  
 1321 -----+-----+-----+-----+-----+-----+ 1380

AACATATTTGACGGCAAAATATCTCGTAGCGAAAACCTACAGTAATCTTTAAATGACTAC  
 1381 -----+-----+-----+-----+-----+-----+ 1440

Fig. 3

Repeat 1

```

=====>
1441 TGTAGCGCTTGTGTCGATTACGGGCTCAATTTTGGAAAATAATTTTTTTTTTCGAATTT 1500
-----+-----+-----+-----+-----+-----+
=====
1501 TGATAACCCGTAAATCGTCACAACGCTACAGTAGTCATTTARAGGATTACTGTAGTTCTA 1560
-----+-----+-----+-----+-----+-----+
1561 GCTACGAGATATTTTGC GCGCCAAATATGACTGTAATACGCATTCTCTGAATTTTGTGTT 1620
-----+-----+-----+-----+-----+-----+
1621 TCCGTAATAATTTTACAAGATTTTGGCATTCCACTTTTAAAGGCGCACAGGATTTATTCCA 1680
-----+-----+-----+-----+-----+-----+
1681 ATGGGTCTCGGCACGCAAAAAGTTTGATAGACTTTTAAATTCTCCTTGCATTTTAAATTC 1740
-----+-----+-----+-----+-----+-----+
1741 AATTACTAAAATTTTCGTGAATTTTCTGTAAAATTTTAAATCAGTTTCTAATATT 1800
-----+-----+-----+-----+-----+-----+
1801 TTCCAGGCTGACAAACAGAAACAAAACACAACAAACATTTTAAAAATCAGTTTCAAAT 1860
-----+-----+-----+-----+-----+-----+
1861 TAAAAATAACGATTTTCTCATTGAAAATTGTGTTTTATGTTTGC GAAAATAAAAGAGAACT 1920
-----+-----+-----+-----+-----+-----+
1921 GATTCAAAACAATTTTAAACAAAAAAAACCCCAAAATTCGCCAGAAATCAAGATAAAAAA 1980
-----+-----+-----+-----+-----+-----+
1981 TTCAAGAGGGTCAAATTTTCCGATTTTACTGACTTTCACCTTTTTTTTCGTAGTTCAGT 2040
-----+-----+-----+-----+-----+-----+
2041 GCAGTTGTTGGAGTTTTTACGAAAAC TAGGAAAAAATCGATAAAAATTACTCAAATCG 2100
-----+-----+-----+-----+-----+-----+
2101 AGCTGAATTTTGAGGACAATGTTTAAAAAAAACACTATTTTCCAATAATTTCACTCAT 2160
-----+-----+-----+-----+-----+-----+

-----
TTTCAGACTAAATCGAAAATCAAATCGTACTCTGACTACGGGTCAGTAGAGAGGTCAACC
-----

2161 -----+-----+-----+-----+-----+-----+ 2220
2221 ATCAGCCGAAGATGATGCGTCAAGATAGAAGGAGCTTGCTAGAGAGGAACATTATGATGT 2280
-----+-----+-----+-----+-----+-----+
          M M R Q D R R S L L E R N I M M F
          1                                10

          T(nl040)
          |
2281 TCTCTAGTCATCTAAAAGTCGATGAAATTCTCGAAGTTCTCATCGCAAAACAAGTGTGTA 2340
-----+-----+-----+-----+-----+-----+
          S S H L K V D E I L E V L I A K Q V L N
          20                                30

          |intron 1
2341 ATAGTGATAATGGAGATATGATTAATGTGAGTTTTTAATCGAATAATAATTTTAAAAAAA 2400
-----+-----+-----+-----+-----+-----+
          S D N G D M I N
          40

          |
2401 AATTGATAATATAAGAATATTTTGCAGTCATGTGGAACGGTTCGCGAGAAGAGACGGG 2460
-----+-----+-----+-----+-----+-----+
                                S C G T V R E K R R E
                                50

```

Fig. 3 (cont.)

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A(n718)

AGATCGTGAAAGCAGTGCAACGACGGGAGATGTGGCGTTCGACGCGTTTTATGATGCTC  
2461 -----+-----+-----+-----+-----+ 2520  
I V K A V Q R R G D V A F D A F Y D A L  
60 70

| intron 2

TTCGCTCTACGGGACACGAAGGACTTGCTGAAGTTCTTGAACCTCTCGCCAGATCGTAGG  
2521 -----+-----+-----+-----+-----+ 2580  
R S T G H E G L A E V L E P L A R S  
80 90

TTTTTAAAGTTCGGCGCAAAAGCAAGGGTCTCACGGAAAAAAGAGGCGGATCGTAATTTT  
2581 -----+-----+-----+-----+-----+ 2640  
GCAACCCACCGGCACGGTTTTTTTCTCCGAAAATCGGAAATTATGCACTTTCCCAAATAT  
2641 -----+-----+-----+-----+-----+ 2700  
TTGAAGTGAAATATATTTTATTTACTGAAAGCTCGAGTGATTATTTATTTTAAACACTA  
2701 -----+-----+-----+-----+-----+ 2760  
ATTTTCGTGGCGCAAAAGGCCATTTTGTAGATTGCGGAAAATACTTGTCACACACACAC  
2761 -----+-----+-----+-----+-----+ 2820

|

ACACACATCTCCTTCAAATATCCCTTTTCCAGTGTTGACTCGAATGCTGTCGAATTCGA  
2821 -----+-----+-----+-----+-----+ 2880  
V D S N A V E F E  
100

GTGTCCAATGTCACCGGCAAGCCATCGTCGGAGCCGCGCATTGAGCCCCGCCGGCTACAC  
2881 -----+-----+-----+-----+-----+ 2940  
C P M S P A S H R R S R A L S P A G Y T  
110 120

TTCACCGACCCGAGTTCACCGTGACAGCGTCTCTTCAGTGTCATTCATTCACTTCTTATCA  
2941 -----+-----+-----+-----+-----+ 3000  
S P T R V H R D S V S S V S S F T S Y Q  
130 140

GGATATCTACTCAAGAGCAAGATCTCGTTCTCGATCGCGTGCACTTCATTCATCGGATCG  
3001 -----+-----+-----+-----+-----+ 3060  
D I Y S R A R S R S R S R A L H S S D R  
150 1 60

| intron 3

ACACAATTATTCATCTCCTCCAGTCAACGCATTTCCAGCCAACCTTGATGTTGATGCG  
3061 -----+-----+-----+-----+-----+ 3120  
H N Y S S P P V N A F P S Q P S  
170

Repeat 1

=====

AACACTAAATTCTGAGAATGCGCATTACTCAACATATTTGACGCGCAAATATCTCGTAGC  
3121 -----+-----+-----+-----+-----+ 3180

=====

GAAAAATACAGTAACCCCTTTAAATGACTATTGTAGTGTGATTTACGGGCTCGATTTTCG  
3181 -----+-----+-----+-----+-----+ 3240

Fig. 3 (cont.)

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==>
3241 AAACGAATATATGCTCGAATTGTGACAACGAATTTTAATTTGTCATTTTTGTGTTTTCTT 3300
-----+-----+-----+-----+-----+-----+

Repeat 1
<=====
3301 TTGATATTTTTGATCAATTAATAAATTATTTCCGTAAACAGACACCAGCGCTACAGTACT 3360
-----+-----+-----+-----+-----+-----+

=====
3361 CTTTTAAAGAGTTACAGTAGTTTTTCGCTTCAAGATATTTTGAAAAGAATTTTAAACATTT 3420
-----+-----+-----+-----+-----+-----+
3421 TGAAAAAAAATCATCTAACATGTGCCAAAACGCTTTTTTCAAGTTTCGCAGATTTTTTGA 3480
-----+-----+-----+-----+-----+-----+

Repeat 2
=====
3481 TTTTTTTCATTCAAGATATGCTTATTAACACATATAATTATCATTAAATGTGAATTTCTTG 3540
-----+-----+-----+-----+-----+-----+

=====
3541 TAGAAATTTGGGCTTTTCGTTCTAGTATGCTCTACTTTTGAAATTGCTCAACGAAAAAA 3600
-----+-----+-----+-----+-----+-----+

=====
3601 TCATGTGGTTTGTTTCATATGAATGACGAAAAATAGCAATTTTTTATATATTTTCCCCTAT 3660
-----+-----+-----+-----+-----+-----+

=====
3661 TCATGTTGTGCAGAAAAATAGTAAAAAAGCGCATGCATTTTTTCGACATTTTTTACATCGA 3720
-----+-----+-----+-----+-----+-----+

=====>
3721 ACGACAGCTCACTTCACATGCTGAAGACGAGAGACGCGGAGAAATACCACACATCTTTCT 3780
-----+-----+-----+-----+-----+-----+

Repeat 2
<=====
3781 GCGTCTCTCGTCTTCAGCATGTGAAATGGGATCTCGGTTCGATGTAAAAAATGTCAATA 3840
-----+-----+-----+-----+-----+-----+

=====
3841 ATGTAAAAAATGCATGCGTTTTTTTTACACTTTTCTGCACAAATGAATAGGGGGAAAATGT 3900
-----+-----+-----+-----+-----+-----+

=====
3901 ATTAAAATACATTTTTTTGTATTTTTCAACATCACATGATTAACCCCATTTTTCGTT 3960
-----+-----+-----+-----+-----+-----+

=====
3961 GAGCAACTTAAAAAGTAGAGAATATTAGAGCGAAAACCAAATTTCTTCAAGATATTACC 4020
-----+-----+-----+-----+-----+-----+

=====
4021 TTTATTGATAATTATAGATGTTAATAAGCATATCTTGAATGAAAGTCAGCAAAAATATGT 4080
-----+-----+-----+-----+-----+-----+

```

Fig. 3 (cont.)

0908243-063201  
102290-1428860

4081 -----+-----+-----+-----+-----+-----+ 4140  
 TTTTTCGATTTTCTACATCACATGAATGTAGAAAATTAAAAGGGAAATCAAAATTTCTA  
 4141 -----+-----+-----+-----+-----+-----+ 4200  
 GAGGATATAATTGAATGAAACATTGCGAAATTAAAATGTGCGAAACGTCAAAAAAGAGGA  
 4201 -----+-----+-----+-----+-----+-----+ 4260  
  
 AATTTGGGTATCAAAATCGATCCTAAAACCAACACATTTTCAGCATCCGCCAACTCTTCAT  
 4261 -----+-----+-----+-----+-----+-----+ 4320  
 S A N S S F  
 180  
  
 TCACCGGATGCTCTTCTCTCGGATACAGTTCAAGTCGTAATCGCTCATTTCAGCAAAGCTT  
 4321 -----+-----+-----+-----+-----+-----+ 4380  
 T G C S S L G Y S S S R N R S F S K A S  
 190 200  
  
 CTGGACCAACTCAATACATATTCATGAAGAGGATATGAACTTTGTCGATGCACCAACCA  
 4381 -----+-----+-----+-----+-----+-----+ 4440  
 G P T Q Y I F H E E D M N F V D A P T I  
 210 220  
  
 TAAGCCGTGTTTTTCGACGAGAAAACCATGTACAGAACTTCTCGAGTCCTCGTGGAATGT  
 4441 -----+-----+-----+-----+-----+-----+ 4500  
 S R V F D E K T M Y R N F S S P R G M C  
 230 240  
  
 GCCTCATCATAAATAATGAACACTTTGAGCAGATGCCAACACGGAATGGTACCAAGGCCG  
 4501 -----+-----+-----+-----+-----+-----+ 4560  
 L I I N N E H F E Q M P T R N G T K A D  
 250 260  
  
 ACAAGGACAATCTTACCAATTTGTTTCAGATGCATGGGCTATACGGTTATTTGCAAGGACA  
 4561 -----+-----+-----+-----+-----+-----+ 4620  
 K D N L T N L F R C M G Y T V I C K D N  
 270 280  
  
 | intron 4  
 ATCTGACGGGAAGGGTACGGCGAAATTATATTACCCAAACGCGAAATTTGCCATTTTGCG  
 4621 -----+-----+-----+-----+-----+-----+ 4680  
 L T G R  
  
 Repeat 3  
 =====>  
 CCGAAAATGTGGCGCCCGGTCTCGACACGACAATTTGTGTTAAATGCAAAAATGTATAAT  
 4681 -----+-----+-----+-----+-----+-----+ 4740  
 TTTGCAAAAAACAAAATTTTGAAGTTCCGCGAAAATGATTTACCTAGTTTCGAAATTTTC  
 4741 -----+-----+-----+-----+-----+-----+ 4800  
 GTTTTTTCCGGCTACATTATGTGTTTTTTCTTAGTTTTTTCTATAATATTTGATGTAAAAA  
 4801 -----+-----+-----+-----+-----+-----+ 4860  
 ACCGTTTGTAATTTTCAGACAATTTCCGCATACAAAACCTTGATAGCAGAAATCAATT  
 4861 -----+-----+-----+-----+-----+-----+ 4920  
 TTCTGAATTTTCAAAATTATCCAAAATGCACAATTTAAAATTTGTGAAAATTGGCAAAC  
 4921 -----+-----+-----+-----+-----+-----+ 4980

Fig. 3 (cont.)

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GGTGTTC AATATGAAATGTATTTTTTAAAACTTTAAAAACCACTCCGGAAGCAATAA
4981 -----+-----+-----+-----+-----+-----+ 5040
AAATCAAAACAACGTCACAATTCAAATTCAAAAGTTATTCATCCGATTTGTTTATTTTTG
5041 -----+-----+-----+-----+-----+-----+ 5100
CAAAATTTGAAAAAATCATGAAGGATTTAGAAAAGTTTATAACATTTTTTCTAGATTTT
5101 -----+-----+-----+-----+-----+-----+ 5160
TCAAAATTTTTTTTAAACAAATCGAGAAAAAGAGAATGAAAAATCGATTTTAAAAATATCC
5161 -----+-----+-----+-----+-----+-----+ 5220

Repeat 3
<=====
ACAGCTTCGAGAGTTTGAAATTACAGTACTCCTTAAAGGCGCACACCCCATTTGCATTGG
5221 -----+-----+-----+-----+-----+-----+ 5280

=====
ACCAAAAAATTTGTCGTGTCGAGACCAGGTACCGTAGTTTTTGTGCGCAAAAATTCACCAT
5281 -----+-----+-----+-----+-----+-----+ 5340
TGGACAATAAACCTTCCTAATCACCAAAAAGTAAAATTGAAATCTTCGAAAAGCCAAAAA
5341 -----+-----+-----+-----+-----+-----+ 5400
ATTCAAAAAAAAAGTCGAATTTTCGATTTTTTTTTTTGGTTTTTTGGTCCCAAAACCAAAA
5401 -----+-----+-----+-----+-----+-----+ 5460
AAATCAATTTTCTGCAAAATACCAAAAAGAAACCCGAAAAAATTTCCCAGCCTTGTTCCCT
5461 -----+-----+-----+-----+-----+-----+ 5520

AATGTAAACTGATATTTAATTTCCAGGGAATGCTCCTGACAATTCGAGACTTTGCCAAAC
5521 -----+-----+-----+-----+-----+-----+ 5580
                        G M L L T I R D F A K H
                        290                        300

ACGAATCACACGGAGATTCTGCGATACTCGTGATTCTATCACACGGAGAAGAGAATGTGA
5581 -----+-----+-----+-----+-----+-----+ 5640
    E S H G D S A I L V I L S H G E E N V I
                        310                        320
TTATTGGAGTTGATGATATACCGATTAGTACACAGAGATATATGATCTTCTCAACGCGG
5641 -----+-----+-----+-----+-----+-----+
    I G V D D I P I S T H E I Y D L L N A A
                        330                        340

                                                A(n2433)
                                                | |
CAAATGCTCCCCGTCTGGCGAATAAGCCGAAAATCGTTTTTGTGCGAGGCTTGTCGAGGCG
5701 -----+-----+-----+-----+-----+-----+ 5760
    N A P R L A N K P K I V F V Q A C R G E
                        350                        360

GTTTCGTTTTTTATTTTAATTTTAATATAAATATTTTAAATAAATTCATTTTCAGAACGTC
5761 -----+-----+-----+-----+-----+-----+ 5820
                                                R R

GTGACAATGGATTCCCAGTCTTGATTCTGTGCGACGGAGTTCCTGCATTTCTTCGTCGTG
5821 -----+-----+-----+-----+-----+-----+ 5880
    D N G F P V L D S V D G V P A F L R R G
                        370                        380

```

Fig. 3 (cont.)



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T(n1165)

GATGGGACAATCGAGACGGGCCATTGTTCAATTTTCTTGGATGTGTGCGGCCGCAAGTTC  
 5881 -----+-----+-----+-----+-----+-----+-----+ 5940  
           W  D  N  R  D  G  P  L  F  N  F  L  G  C  V  R  P  Q  V  Q  
                                   390                                  400

      | intron 6  
 AGGTTGCAATTTAATTTCTTGAATGAGAATATTCCTTCAAAAAATCTAAAATAGATTTTT  
 5941 -----+-----+-----+-----+-----+-----+ 6000  
 ATTCCAGAAAGTCCCGATCGAAAAATTGCGATATAATTACGAAATTTGTGATAAAATGAC  
 6001 -----+-----+-----+-----+-----+-----+ 6060

      Repeat 4  
 =====  
 AAACCAATCAGCATCGTCGATCTCCGCCCACTTCATCGGATTGGTTTGAAAGTGGGCGGA  
 6061 -----+-----+-----+-----+-----+-----+ 6120

=====>  
 GTGAATTGCTGATTGGTCGCAGTTTTTCAGTTTAGAGGGAATTTAAAAATCGCCTTTTCGA  
 6121 -----+-----+-----+-----+-----+-----+ 6180  
 AAATTAAAAATTGATTTTTTCAATTTTTTCGAAAAATATTCGATTATTTTATATTCTTT  
 6181 -----+-----+-----+-----+-----+-----+ 6240

A(n717)

GGAGCGAAAGCCCCGTCCTGTAAACATTTTTAAATGATAATTAATAAATTTTGCAGCAA  
 6241 -----+-----+-----+-----+-----+-----+ 6300  
   Q

T(n1949)

GTGTGGAGAAAGAAGCCGAGCCAAGCTGACATTCTGATTTCGATACGCAACGACAGCTCAA  
 6301 -----+-----+-----+-----+-----+-----+ 6360  
   V  W  R  K  K  P  S  Q  A  D  I  L  I  R  Y  A  T  T  A  Q  
                                   410                                  420

A(n1286)

TATGTTTCGTGGAGAAACAGTGCTCGTGGATCATGGTTCATTCAAGCCGTCTGTGAAGTG  
 6361 -----+-----+-----+-----+-----+-----+ 6420  
   Y  V  S  W  R  N  S  A  R  G  S  W  F  I  Q  A  V  C  E  V  
                                   430                                  440

T(n1129,n1164)

TTCTCGACACACGCAAAGGATATGGATGTTGTTGAGCTGCTGACTGAAGTCAATAAGAAG  
 6421 -----+-----+-----+-----+-----+-----+ 6480  
   F  S  T  H  A  K  D  M  D  V  V  E  L  L  T  E  V  N  K  K  
                                   450                                  460

T(n2430)

A(n2426)

      | intron 7  
 GTCGCTTGTGGATTTTCAGACATCACAGGGATCGAATATTTTGAAACAGATGCCAGAGGTA  
 6481 -----+-----+-----+-----+-----+-----+ 6540  
   V  A  C  G  F  Q  T  S  Q  G  S  N  I  L  K  Q  M  P  E  
                                   470                                  480

Fig. 3 (cont.)

T02290" CH28860

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                                Repeat 5
                                =====
6541 CTTGAAACAAACAATGCATGTCTAACTTTTAAGGACACAGAAAATAGGCAGAGGCTCCT 6600
-----+-----+-----+-----+-----+-----+

=====>
6601 TTTGCAAGCCTGCCGCGCTCAACCTAGAATTTTAGTTTTAGCTAAAATGATTGATTTT 6660
-----+-----+-----+-----+-----+-----+
6661 GAATATTTTATGCTAATTTTTTTTTCGTTAAATTTTGAAATAGTCACTATTTATCGGGTTT 6720
-----+-----+-----+-----+-----+-----+
6721 CCAGTAAAAAATGTTTATTAGCCATTGGATTTTACTGAAAACGAAAATTTGTAGTTTTTTC 6780
-----+-----+-----+-----+-----+-----+
6781 AACGAAATTTATCGATTTTTTAAATGTAAAAAAAATAGCGAAAATTACATCAACCATCAA 6840
-----+-----+-----+-----+-----+-----+
6841 GCATTTAAGCCAAAATTGTTAACTCATTTAAAAATTAATTCAAAGTTGTCCACGAGTATT 6900
-----+-----+-----+-----+-----+-----+

                                Repeat 5
                                <=====
6901 ACACGGTTGGCGCGCGGCAAGTTTGCAAACGACGCTCCGCCTCTTTTTCTGTGCGGCTT 6960
-----+-----+-----+-----+-----+-----+

=====
6961 GAAAACAAGGGATCGGTTTAGATTTTTCCCAAATTTAAATTAAATTTTCTGATGACATC 7020
-----+-----+-----+-----+-----+-----+
                                M T S
                                T(n1163)

7021 CCGCCTGCTCAAAAAGTTCTACTTTTTGGCCGGAAGCACGAAACTCTGCCGTCTAAAATTC 7080
-----+-----+-----+-----+-----+-----+
      R L L K K F Y F W P E A R N S A V *
      490                                500

7081 ACTCGTGATTCATTGCCCAATTGATAATTGTCTGTATCTTCTCCCCCAGTTCTCTTTCGC 7140
-----+-----+-----+-----+-----+-----+
7141 CCAATTAGTTTAAAACCATGTGTATATTGTTATCCTATACTCATTTCACTTTATCATTCT 7200
-----+-----+-----+-----+-----+-----+
7201 ATCATTTCTCTTCCCATTTTACACATTTCCATTTCTCTACGATAATCTAAAATTATGAC 7260
-----+-----+-----+-----+-----+-----+
7261 GTTTGTGTCTCGAACGCATAATAATTTAATAACTCGTTTTGAATTTGATTAGTTGTTGT 7320
-----+-----+-----+-----+-----+-----+
7321 GCCCAGTATATATGTATGTACTATGCTTCTATCAACAAAATAGTTTCATAGATCATCACC 7380
-----+-----+-----+-----+-----+-----+
7381 CCAACCCACCAACCTACCGTACCATATTCATTTTTTGC CGGAATCAATTTGATTAATT 7440
-----+-----+-----+-----+-----+-----+
7441 TTAACCTATTTTTTCGCCACAAAAAATCTAATATTTGAATTAACGAATAGCATTCCCATC 7500
-----+-----+-----+-----+-----+-----+
7501 TCTCCCGTGCCGGAATGCCTCCCGGCCTTTTAAAGTTTCGGAACATTTGGCAATTATGTAT 7560
-----+-----+-----+-----+-----+-----+
7561 AAATTTGTAGGTCCCCCCCATCATTTCCCGCCCATCATCTCAAATTGCATTCTTTTTTCG 7620
-----+-----+-----+-----+-----+-----+
7621 CCGTGATATCCCGATTCTGGTCAGCAAAGATCT 7653
-----+-----+-----+-----+-----+

```

Fig. 3 (cont.)

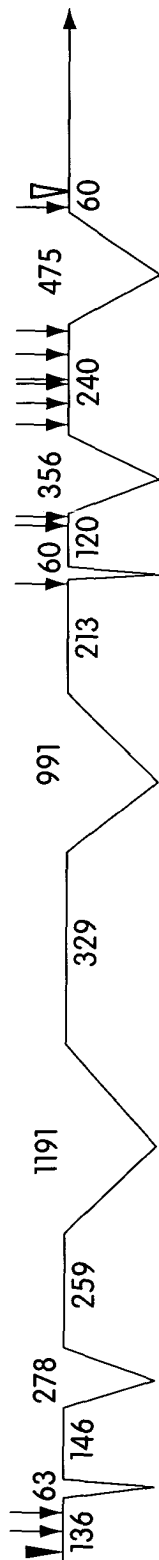


Fig. 4A

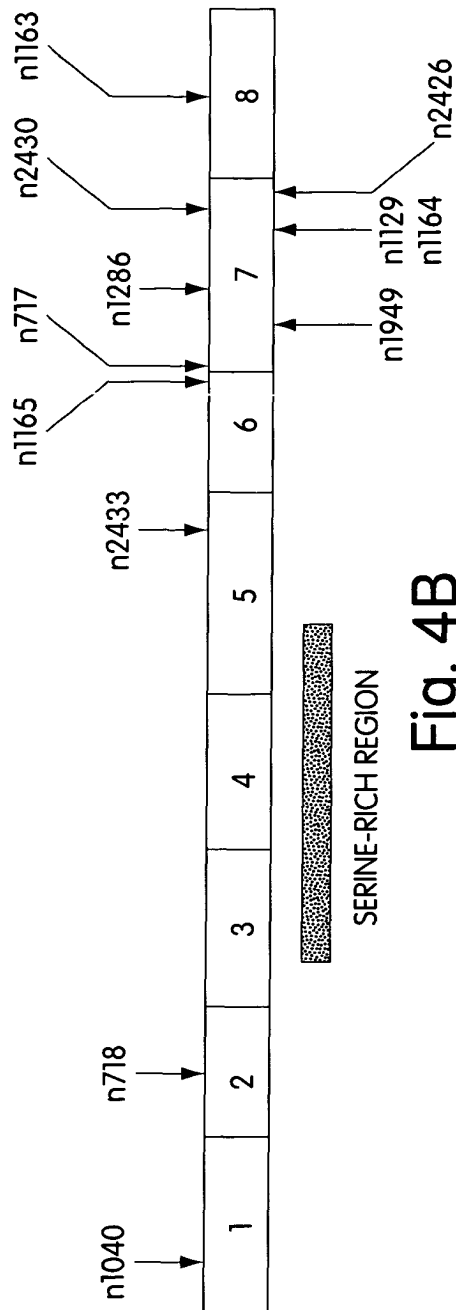


Fig. 4B

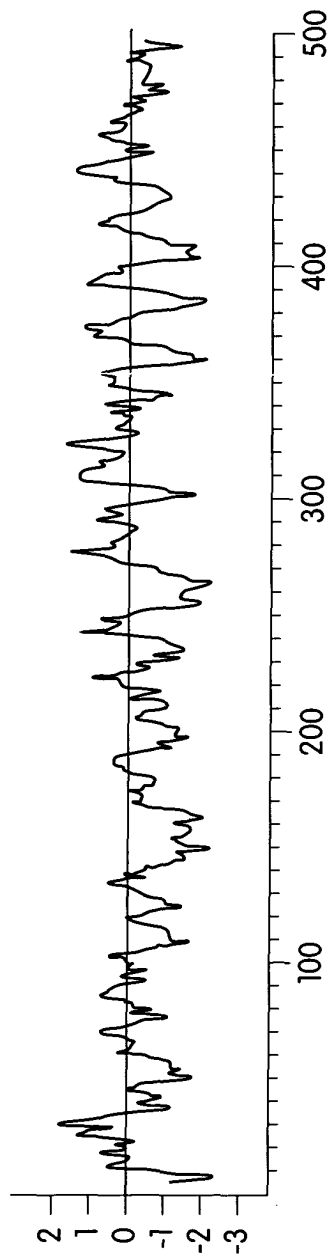


Fig. 5

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# Alignment of ced-3 and Human Interleukin -1 $\beta$ convertase

ICE	1	MADKVLKEKRKLFIRSM....GEGTINGLLDELLQTRVLNKEEMEKVKRE
		: : : :   :   :   : : : :   :   : : :   : : : : .
Ced-3	1	...MMRQDRRSLLERNIMMFSSHLKVDEILEVLIQVLNSDNGDMIN.S
		↓ F
BGAFQ		=====
PBA		=====
	47	NATVMDKTRALIDSVIPKGAQACQ.ICITYICEEDSYLAGTLGLSADQTS
		:   : :     : : : :   :   :   : : : :   : :   :   : .
	47	CGTVREKRREIVKAVQRPQDVAFDAFYDALRSTGHEGLAEVLEPLARSVD
		↓ R
BFAFQ		=====
PBA		=====
	96	GNYLNMQ.....DSQGVLSFF.....
		:   : : : : : : : : : :   : : :
	97	<u>SNAVEFECPMSPASHRRSRALSPAGYTSPTVRHRDSVSSVSSFTSYODIY</u>
		serine-rich region
BGAFQ		=====
PBA		=====
	112	.....PAPQAVQDNPAMPTSSGSEGNVKLCSLE
		: :   : :   : :   : :   : :   : :
	147	<u>SRARSRSRSLHSSDRHNYSSPPVNAFPSOPSSANSSTGCSSLGYSS</u>
BGAFQ		=====
PBA		===
	140	EAQRIWKQKSAEIYPIMDK.....SSRTRLAL
		: : : :   : : : :   : : : :   : : : :   : : : :
	197	<u>RNRSFSKASGPTQYIFHEEDMNFVDAPTISR VFDEKTM YRNFS SPRGMCL</u>
BGAFQ		=====

Fig. 6A

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ICE 167 IICNEEFDSIPRRTGAEVDITGMTMLLQNLGYSDVKKNLTASDMTTELE  
 || |||. |: :| |. |...| ..:| |:. :|||. |. | |||: :| :.  
 Ced-3 247 IINNEHF EQMPTRNGTKADKDNLTNLFRCMGYTVICKDNLTGRGMLLTIR  
 BGAFQ =====

217 AFAHRPEHKTS DSTFLVFM SHGIREGICGKKHSEQVPDI.LQLNAIFNML  
 .| |. :...| :|||. :||| :||| :..|. |. | | : :. | : : :|  
 297 DFAKHESH..GDSAILVILSHGEENVIG.....VDDIPISTHEIYDLL

BGAFQ =====

active site autocleavage site  
 266 NTKNCPSLKDKPKV IIIQACRGDSPGVVW.FKDSVGVSGNLSLPTTEEFE  
 |. |. |. | :|||: :||| :||| :...: ..: . |||: . : : .. : : :  
 339 NAANAPRLANKPKIVFVQACRGERRDNGFPVLDSVDGVPAFLRRGWDNRD

↓  
 S

BGAFQ =====

315 DDAI.....KKAHIEKDFIAFCSTPDNVSWRHPTMGSVFI  
 :. : :| . : |:: :..|:: |||: :...| |||  
 389 GPLFNFLGCVRPQVQVWRKKPSQADILIRYATTAQYVSWRNSARGSWFI  
 ↓ ↓  
 stop stop

351 GRLIEHMQEYACSCDVEEIF....RKVRFSFEQPDGRAQMPTT.ERVT.L  
 . :. | : ..| . || |:: :|| :|: :..|.. :. | :. |  
 439 QAVCEVFSTHAKDMDVVELL TEVNKKVACGFQTSQGSN ILKQMP EMTSRL  
 ↓ ↓ ↓ ↓  
 V V K F

395 TRCFYLFPGH\*..... 404  
 : ||::|:  
 489 LKKFYFWPEARNSAV 503

Fig. 6A (cont.)

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 T02290-E428880



# Alignment of N-terminal regions of ced-3/ICE- related proteins

c. briggsae ced-3	MMQDRWLLERNILEFSSKLQADLILDVLIQVLSNDGVDVNSCRTERDNEKEIVKAVQRRGDEAFDAFYDALRDTGHNDLADVLMPLSR---PNPV	
ced-3 protein	MMQDRRSLERNIMFSSHLKVDLEVLIAQVLSNDGMDINSCGTVRKHREIVKAVQRPQGVAFDAFYDALRSTGHEGLAEVLEPLARSVDNAV 100	
C. vulgaris ced-3	-----ADKIL-----	
Mouse ICE.gw	M-----RAKKQFINSV---SIGTINGLLDELLEK-----RVLNQDEEM-----DKI	
Human ICE.GW	M-----ADKVL-----KEKKLFIISM---GEGTINGLLDELLEQT-----RVLNKEEM-----EKV	
Consensus	M.....AD.IL.....V...G.....D.L.T.....VL.....V	
c. briggsae ced-3	PMCEPMSPPSHRRSRALSPPGYASPTRVHRDSTSSVSFTSTVDVYSRRSSSRSLQSSDRHNYMSAA-TSFPSPSSANSFTGCASLGYSSSRN	
ced-3 protein	EFECPMSPASHRRSRALSPAGYTSPTVRHRDSTSSVSFTSYQD-IYSRRARSRS-RAIHSSDRHNYSPPVNAFPSPQSSANSFTGCSSLGYSSSRN 198	
C. vulgaris ced-3	-----STSRSSRPLETSDRHNYSVPS-NSFQSQPASANSFTGSSSSLGYSSSRT	
Mouse ICE.gw	KLA---NITAMDKARDLCDHVSXKGPQASQIFTYICNEDCYL-----AGILEQSAPSAE--TFVAT-----EDSKGGHPSSSETKEEQNKED-G	
Human ICE.GW	KRE---NATVMDKTRALIDSVIPKGAQACQICITYICEEDSYL-----AGTIGLSADQTSQ--NYLNM-----QDSQGVLSFPAPQAVQNDPAMP	
Consensus	..E-----RAL.....I.....SY.....S.SRS.R.L.SSDRHNY.S...F.SQP.SANSFTG.-SLGYSSSR.	
c. briggsae ced-3	RSFSEKTSAQSYIFHEEDMNVVDAPTIHRVFDEKTYRNFSSPRGLCLIIINNEHFEQMPTRNGTKADKDNLTNIFRCMGYTVI CKDNLITGREMLSTIRSF	
ced-3 protein	RSFSKASGPTQYIFHEEDMNFVDAPTISRVFDEKTYRNFSSPRGNCLIIINNEHFEQMPTRNGTKADKDNLTNLFRCMGYTVI CKDNLITGRGMLLTIRDF	
C. vulgaris ced-3	RSYSKASASQYIFHEEDMNVVDAPTIHRVFDEKTYRNFSTPRGLCLIIINNEHFEQMPTRNGTKADKDNISNLFRCMGYTVI CKDNLITGRMML-TIRDF	
Mouse ICE.gw	TFPGLTGTLKFCPLEKAQKLWKENPS--EIIY--PIMNTT-TRTR-LALII CNTFFQHLSPRVGAQVLLREMKLLLEDLGYTVKVKENLTALENVKEVKEF	
Human ICE.GW	TSSGSEGNVKLCSLEEAQRIWKQKSA--EIIY--PIMDKS-SRTR-LALII CNEEEDSIPRRITGAEVDTITGMTWLLQNLGYSDVVRKNLTASDMTTTELEAF	
Consensus	RS.SK.S...QYIFHEEDMN.VDAPTI.RVFDEKTYRNFSSPRGLCLIIINNEHFEQMPTRNGTK.DKDN.TNLFRCMGYTVI.QKDNLITGR.ML.TIR.F	
c. briggsae ced-3	GRNDME--GDSAILVTLSHGEENVIIIG---VDDVS--VNVHEITVDLINAANAAPRLANKPKLVFVQACRG	
ced-3 protein	AKHESH--GDSAILVTLSHGEENVIIIG---VDDIP--ISTHEITVDLINAANAAPRLANKPKLVFVQACRG	
C. vulgaris ced-3	AKNETH--GDSAILVTLSHGEENVIIIG---VDDVS--VNVHEITVDLINAANAAPRLANKPKLVFVQACRG	
Mouse ICE.gw	AACPHEKTS DSTFLVFMSHGIGEGICGTTYSNEVSDILKVDITFQMMNTLNCPSLKDKPKVIIIQACRG	
Human ICE.GW	AHRPEKTS DSTFLVFMSHGIGREGICGKKHSEQVPDILQLNALFNMLNTKNCPSLKDKPKVIIIQACRG	
Consensus	A.....H...CDSAILVTLSHGEENVIIIG---VDDVS---VHEITVDLINAANAAPRLANKPKLVFVQACRG	

Fig. 6C

# Alignment of C-terminal regions of ced-3/ICE/NEDD-2 - related proteins

ICE C-terminus	DSPGVW---	-----	--FKDSVG--	-----	-----V
Mouse ICE C-ter	EKGQVL---	-----	--LKDSVR--	-----	-----D
C.briggsae C-ter	ERRDNGFP--	-----	--VLDSDVG--	-----VPSLI	-----RRGWDN
ced-3 Cterminus	ERRDNGFP--	-----	--VLDSDVG--	-----VPAFL	-----RRGWDN 386
C. vulgaris C-terminus	ERRDVGF--	-----	--VLDSDVG--	-----VPALI	-----RRGWDK
nedd-2 protein.gw	MLTVQVYRTS	QKCSSSKHV	EVLLDPLGTS	FCSLLPFLL	LYETDRGVDDQ
Consensus	E.....	-----	--LDSV..	-----P...	-----RG.D.
ICE C-terminus	SGNL----SLP	TTEFE---D	DAIKKA-HIE	KDFIAFCSST	PDNVSWRHPT
Mouse ICE C-ter	SEE----DFL	TDAIFE---D	DGIKKA-HIE	KDFIAFCSST	PDNVSWRHPT
C.briggsae C-ter	RDG-PLFNFL	GCVRPQV--Q	QVWRKK-PSQ	ADMLIAYATT	AQYVSWNSA
ced-3 Cterminus	RDG-PLFNFL	GCVRPQV--Q	QVWRKK-PSQ	ADILLIAYATT	AQYVSWNSA 432
C. vulgaris C-terminus	GDG-P--NFL	GCVRPQA--Q	QVWRKK-PSQ	ADILLIAYATT	AQYVSWNSA
nedd-2 protein.gw	QDGKNTQSP	GCEESDAGKE	ELMKRLPTR	SDMICGYACL	KGNAAMNTK
Consensus	.DG-.---.FL	GC.....	....K.-P..	.D.....YA.T	...VSWEN..
ICE C-terminus	MGSVFIQRLI	EHMQETACSC	DVEEIFRNV-	-RF-----SFE	QPDGRAQMPT
Mouse ICE C-ter	RGSLEFIESLI	KHKKEYAWSC	DLEDIFRNV-	-RF-----SFE	QPEFRLQMPT
C.briggsae C-ter	RGSWFIQAVC	EVFSLHAKDM	DVVELLTFVN	KKVA--CGFQ	TSQGSNILKQ
ced-3 Cterminus	RGSWFIQAVC	EVFSTHAKDM	DVVELLTFVN	KKVA--CGFQ	TSQGSNILKQ 480
C. vulgaris C-terminus	RGSWFIQAVC	EVFSLHAKDM	DVVELLTFVN	KKVA--CGFQ	TSQGANILKQ
nedd-2 protein.gw	RGSWYIEALT	QVFSEACDM	HVADMLVNVN	ALIKEREGYA	PGTEFHRCKE
Consensus	RGS.FI.A..	EVFS..A.DM	DV.E.L..M.	....---GF.	...G.....K.
ICE C-terminus	T-ERVT-LTR	CFYLFPGH--	-----	-----	-----
Mouse ICE C-ter	A-DRVT-LTR	RFYLFPGH--	-----	-----	-----
C.briggsae C-ter	MPELTSRLK	KFYFWPEDRG	RNSAV	-----	-----
ced-3 Cterminus	MPENTSRLK	KFYFWPEAR-	-NSAV	503	-----
C. vulgaris C-terminus	MPELTSRLK	KFYFWPEDRN	RSSAV	-----	-----
nedd-2 protein.gw	MSEYCSILCQ	QLYLFPG---	-YPPT	-----	-----
Consensus	M.E...S.L.K	.FY..P..	---P....	-----	-----

Fig. 6D



Lines

```

1  01  MMRQDRRSLLERNIMMFSSHLKVDEILEVLIQVLNSDNGDMINSCGTV  50
2      .....W_.....LE...K.QA.L..D.....V....R.E
3      TVSISLI..R.....  M.....

1  51  REKRREIVKAVQRPQDVAFDAFYDALRSTGHEGLAEVLEPLARSVDSNAV  100
2      .DNEK.....R..E.....D...ND..D..M..S.P   .P.
3

1  101  EFECPMSPASHRRSRALSPAGYTSPTRVHRDSVSSVSSFTS_YQDIYSRA  149
2      PM.....S.....P .A.....I.....T...V....
3      S

1  150  RSRSR_SRALHSSDRHNYSSPPVNAFPSQPSSANSSFTGCSSLGYSSSRN  198
2      ..S..S..P.Q.....M.AA_TS.....A.....
3      T...__..P..T.....V..S..S.Q...A.....S.....T

1  199  RSFSKASGPTQYIFHEEDMNFVDAPTISR VFDEKTM YRNFSSPRGMCLI  247
2      .....T.AQS.....Y.....H.....L...
3      ..Y....AHS.....Y.....H.....T...L...

1  248  INNEHF EQMPTRNGTKADKDNLTNLFRCMGYTVICKDNLTGRGMLLTIRD  297
2      .....I.....E..S...S
3      .....P....IS.....I.H.....M.....

1  298  FAKHESHGDSAILVILSHGEENV IIGVDDIP ISTHEIYDLLNAANAPRLA  347
2      .GRNDM.....VSVNV.....
3      ...N.T.....VSVNV....x.....

1  348  NKPKIVFVQACRGERRDNGFPVLDSV DGVPAFLRRGWDNRDGPLFNFLGC  397
2      ....L.....SLI.....
3      ....L.....V.....LI.....KG...

1  398  VRPQVQQVWRKKPSQADILIRYATTAQYVSWRNSARGSWFIQAVCEVFST  447
2      .....M..A.....L
3      ....A.....A.....L

1  448  HAKDMDVVELL TEVNKKVACGFQTSQGSNILKQMPEMTSRLLKKFYFWPE  497
2      .....L.....
3      .....A.....L.....

1  498  __ARN__SAV  503
2      DRG..__...
3      __D..RS...

```

Fig. 7

Interleukin-1 $\beta$  convertase cDNA sequence

1 AAAAGGAGAG AAAAGCCATG GCCGACAAGG TCCTGAAGGA GAAGAGAAAG  
 51 CTGTTTATCC GTTCCATGGG TGAAGGTACA ATAAATGGCT TACTGGATGA  
 101 ATTATTACAG ACAAGGGTGC TGAACAAGGA AGAGATGGAG AAAGTAAAC  
 151 GTGAAAATGC TACAGTTATG GATAAGACCC GAGCTTTGAT TGACTCCGTT  
 201 ATTCCGAAAG GGGCACAGGC ATGCCAAATT TGCATCACAT ACATTTGTGA  
 251 AGAAGACAGT TACCTGGCAG GGACGCTGGG ACTCTCAGCA GATCAAACAT  
 301 CTGGAAATTA CCTTAATATG CAAGACTCTC AAGGAGTACT TTCTTCCTTT  
 351 CCAGCTCCTC AGGCAGTGCA GGACAACCCA GCTATGCCCA CATCCTCAGG  
 401 CTCAGAAGGG AATGTCAAGC TTTGCTCCCT AGAAGAAGCT CAAAGGATAT  
 451 GGAAACAAAA GTCGGCAGAG ATTTATCCAA TAATGGACAA GTCAAGCCGC  
 501 ACACGTCTTG CTCTCATTAT CTGCAATGAA GAATTTGACA GTATTCCTAG  
 551 AAGAACTGGA GCTGAGGTTG ACATCACAGG CATGACAATG CTGCTACAAA  
 601 ATCTGGGGTA CAGCGTAGAT GTGAAAAAAA ATCTCACTGC TTCGGACATG  
 651 ACTACAGAGC TGGAGGCATT TGCACACCGC CCAGAGCACA AGACCTCTGA  
 701 CAGCACGTTT CTGGTGTTCA TGTCTCATGG TATTCGGGAA GGCATTTGTG  
 751 GGAAGAAACA CTCTGAGCAA GTCCCAGATA TACTACAACT CAATGCAATC  
 801 TTAAACATGT TGAATACCAA GAACTGCCCA AGTTTGAAGG ACAAACCGAA  
 851 GGTGATCATC ATCCAGGCCT GCCGTGGTGA CAGCCCTGGT GTGGTGTGGT  
 901 TTAAAGATTC AGTAGGAGTT TCTGGAAACC TATCTTTACC AACTACAGAA  
 951 GAGTTTGAGG ATGATGCTAT TAAGAAAGCC CACATAGAGA AGGATTTTAT  
 1001 CGCTTTCTGC TCTTCCACAC CAGATAATGT TTCTTGGAGA CATCCCACAA  
 1051 TGGGCTCTGT TTTTATTGGA AGACTCATTG AACATATGCA AGAATATGCC  
 1101 TGTTCTCTGT ATGTGGAGGA AATTTTCCGC AAGGTTGAT TTTCAATTGA  
 1151 GCAGCCAGAT GGTAAGAGCGC AGATGCCCAC CACTGAAAGA GTGACTTTGA  
 1201 CAAGATGTTT CTACCTCTTC CCAGGACATT AAAATAAGGA AACTGTATGA  
 1251 ATGTCTGCGG GCAGGAAGTG AAGAGATCGT TCTGTAAAAG GTTTTTGGAA  
 1301 TTATGTCTGC TGAATAATAA ACTTTTTTTG AAATAATAAA TCTGGTAGAA  
 1351 AAATGAAAAA AAAAAAAAAA AAA

Fig. 8

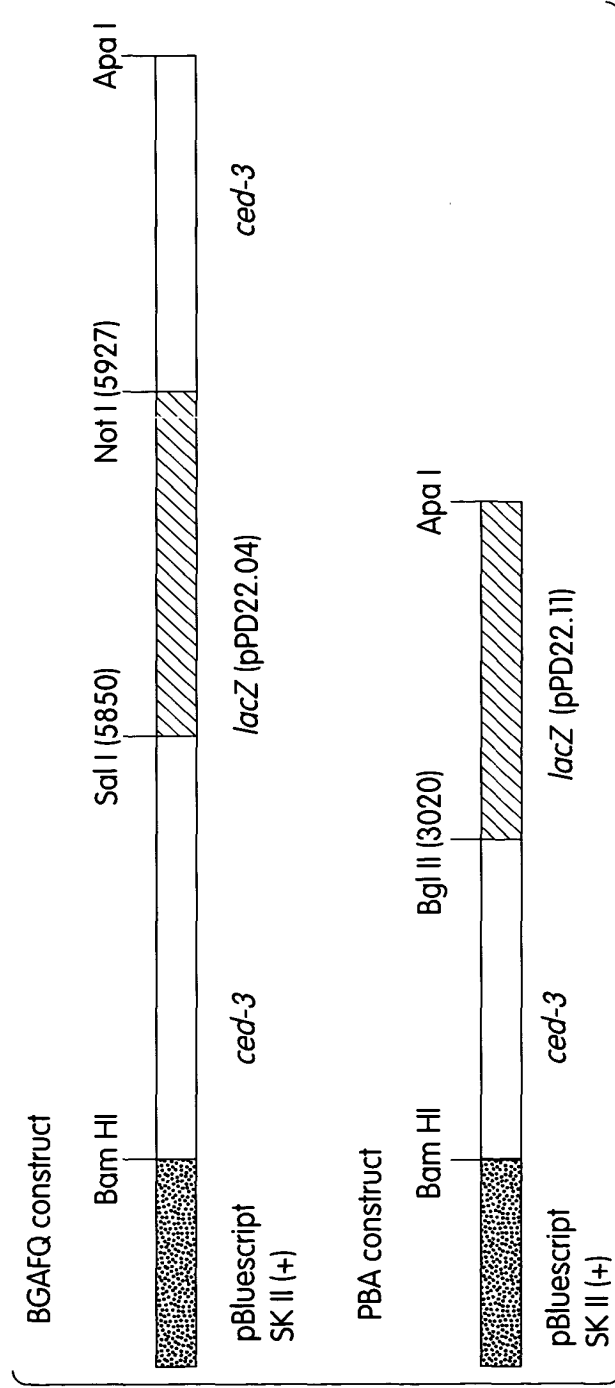


Fig.9A

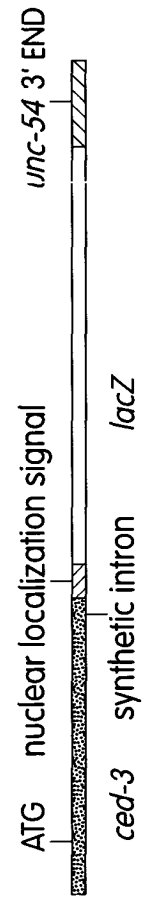


Fig.9B

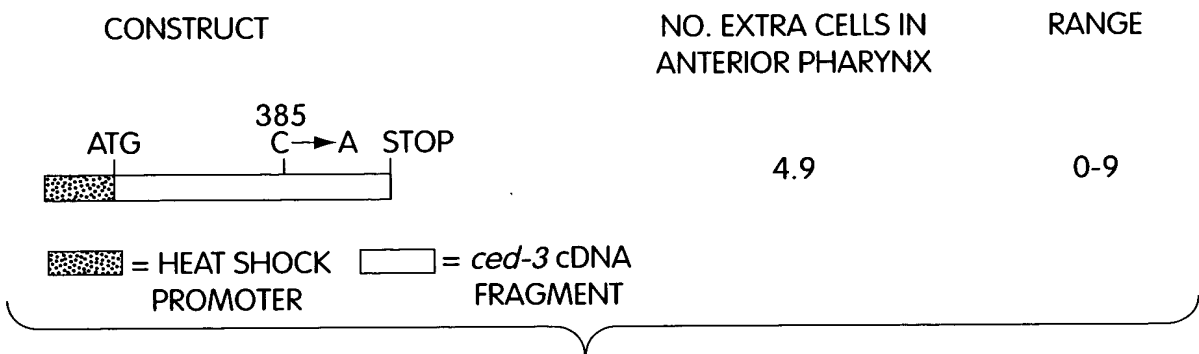


Fig. 10

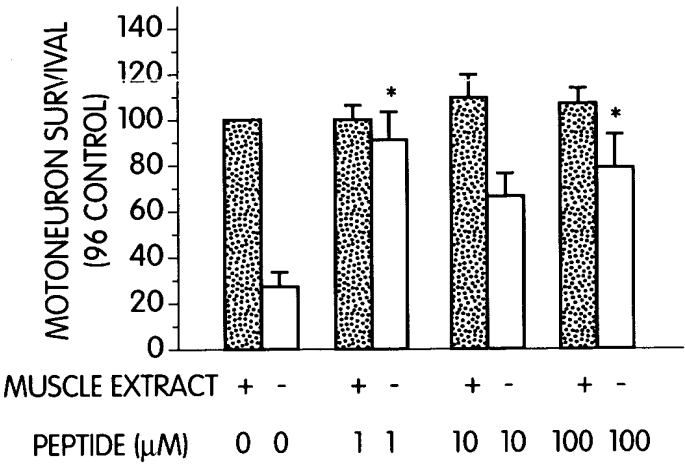


Fig. 11A

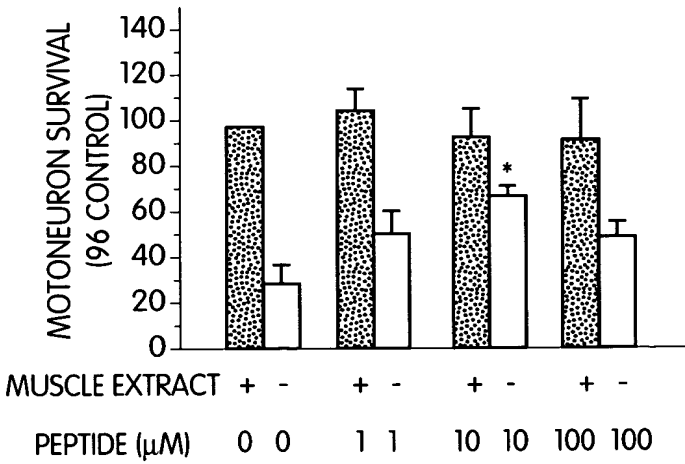


Fig. 11B

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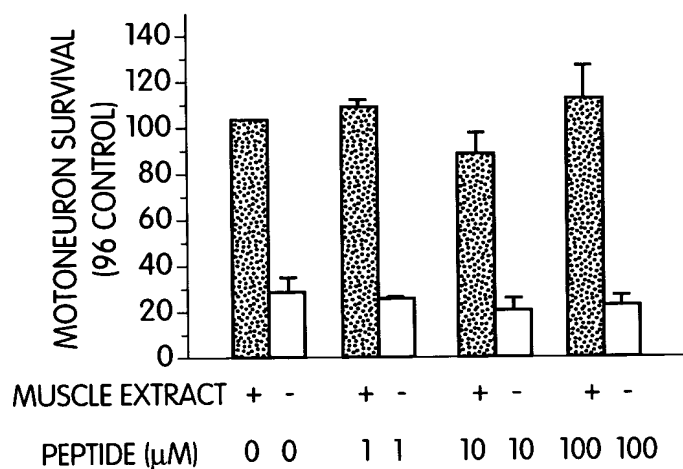


Fig. 11C

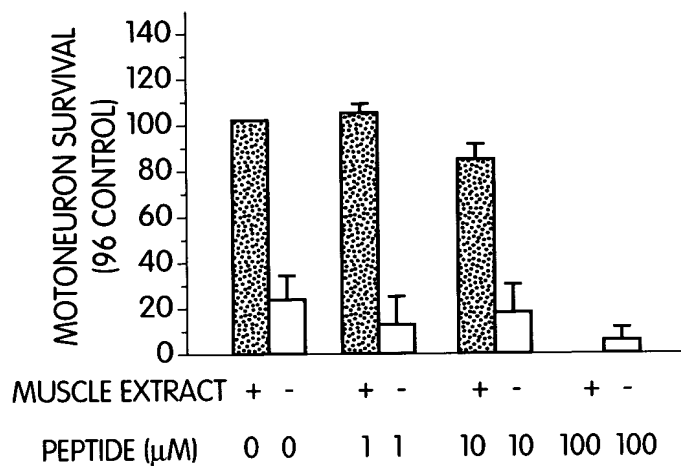


Fig. 11D

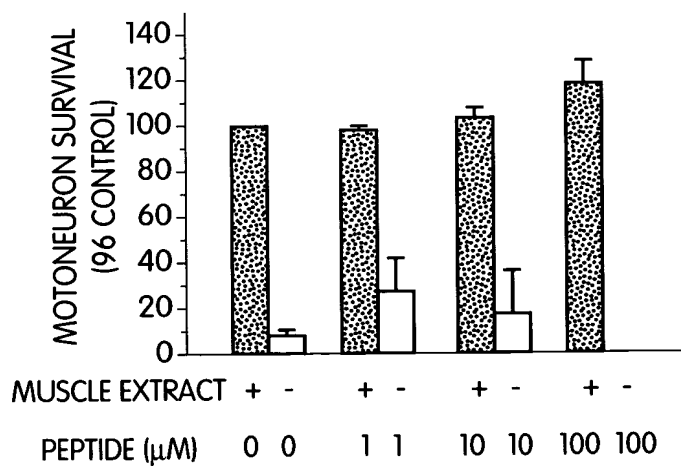
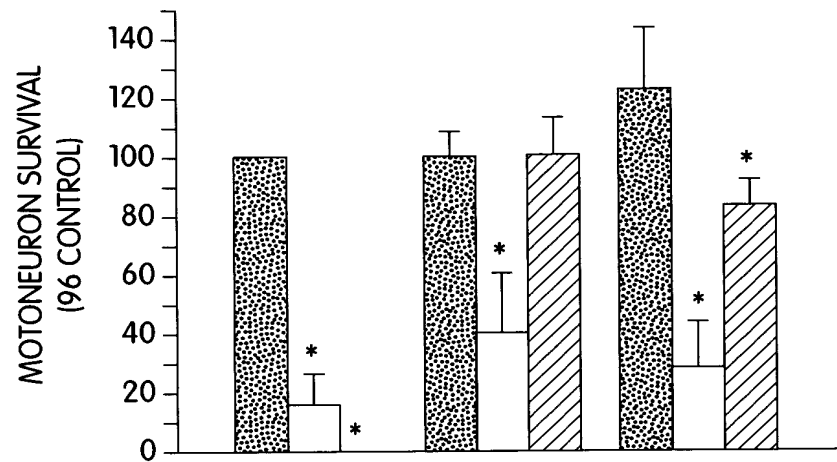
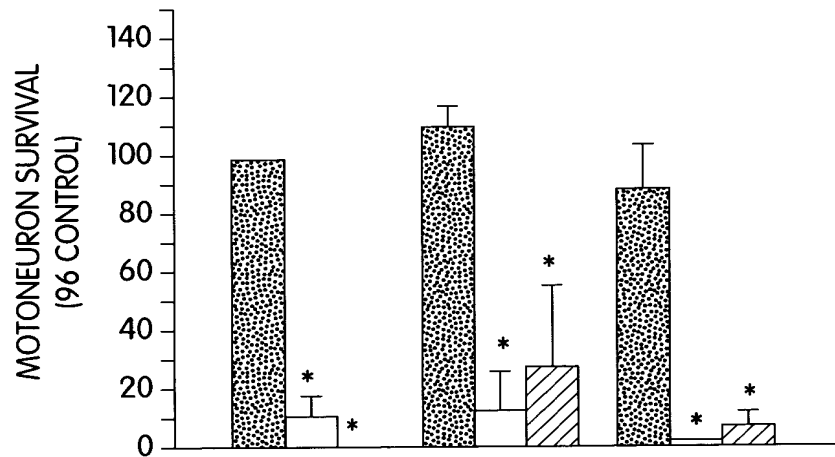


Fig. 11E



MUSCLE EXTRACT AT PLATING	+	-	-	+	-	-	+	-	-
PEPTIDE (μM)	0	0	0	1	1	1	10	10	10
MUSCLE EXTRACT AT 72 Hrs.	-	-	+	-	-	+	-	-	+

Fig. 12A



MUSCLE EXTRACT AT PLATING	+	-	-	+	-	-	+	-	-
PEPTIDE (μM)	0	0	0	1	1	1	10	10	10
MUSCLE EXTRACT AT 72 Hrs.	-	-	+	-	-	+	-	-	+

Fig. 12B

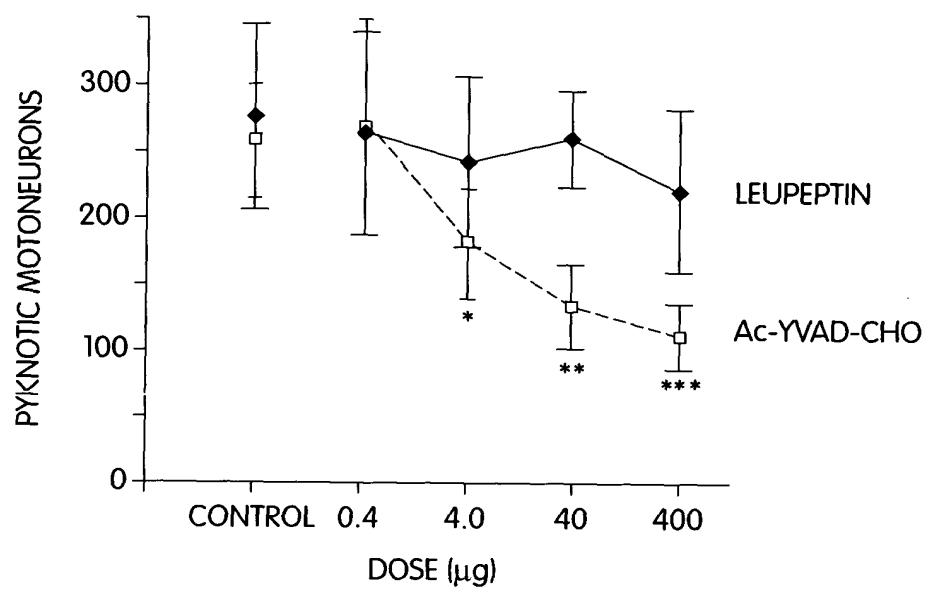


Fig. 13

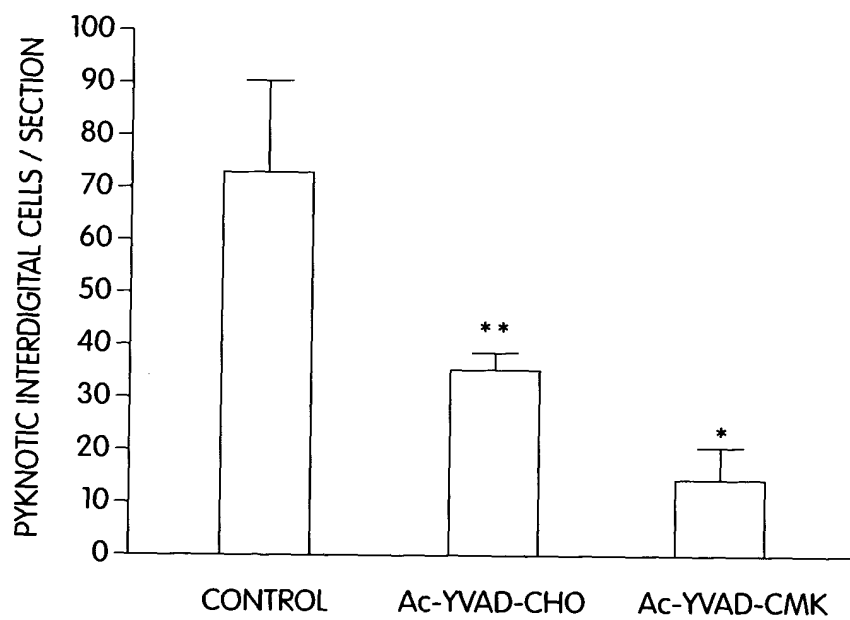


Fig. 14

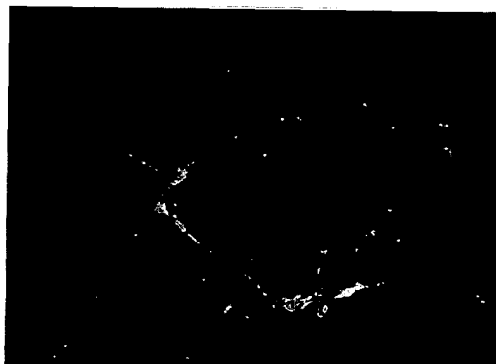


Fig. 15C



Fig. 15D



Fig. 15E



Fig. 15F



Fig. 15G

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FO2290-E428860